

WHAT IS CLAIMED IS:

1. A method for analyzing a computed tomography scan of a whole lung for lung nodules, said method comprising the steps of:

5 (a) segmenting a first lung region and a second lung region from the computed tomography scan, the first lung region corresponding to lung parenchyma of the lung and the second lung region corresponding to at least one of a pleural surface of the lung and a surface defined by vessels within the lung;

10 (b) generating an initial list of nodule candidates from the computed tomography scan within the first lung region, the list including at least a center location and an estimated size associated with each nodule candidate;

(c) generating a subimage for each nodule candidate in the initial list;

15 (d) selectively removing streaking artifacts from the subimage; and

(e) filtering the nodule candidate identified on the initial list to eliminate false positives from the list.

20 2. A method for analyzing a whole lung computed tomography scan as defined in Claim 1, wherein step (b) comprises the substeps of:

(i) thresholding the first lung region;
(ii) labeling high density voxels foreground voxels to identify nodule
25 candidate regions;
(iii) determining for each foreground voxel R_{MI} ;
(iv) selecting the local maximum \hat{R}_{MI} within a nodule candidate region;
(v) determining a limited extent criterion for each foreground voxel which corresponds to a \hat{R}_{MI} ;

(vi) generating the initial list of nodule candidates which satisfy the limited extent criterion, the list including at least N_c and \hat{R}_{MI} associated with the corresponding foreground voxel.

5 3. A method for analyzing a whole lung computed tomography scan as defined in Claim 1, wherein step (d) comprises the substeps of:

(i) determining an amount of streaking artifact present in the sub-image;
and

10 (ii) filtering the streaking artifact out from the subimage when the amount of the streaking artifact present in the sub-image exceeds T_{sar} .

4. A method for analyzing a whole lung computed tomography scan as defined in Claim 3, wherein the amount of streaking artifact present in the sub-image is
15 calculated by a metric

$$S_m = \frac{1}{nmp} \sum_i^n \sum_j^m \sum_k^p (I(i,j,k) - I(i,j+1,k))^2$$

5. A method for analyzing a whole lung computed tomography scan as defined in
20 Claim 3, wherein the filtering is performed by a vertical median filter of size 1x3.

6. A method for analyzing a whole lung computed tomography scan as defined in Claim 3, wherein T_{sar} is from about 20000 to about 80000.

25 7. A method for analyzing a whole lung computed tomography scan as defined in Claim 1, wherein step (e) comprises the substeps of:

(i) determining for each nodule candidate a fraction, F_a , a surface of the nodule candidate that is attached to other solid structures; and

30 (ii) removing the nodule candidate from the list when the fraction exceeds T_a .

8. A method for analyzing a whole lung computed tomography scan as defined in Claim 1, wherein step (e) comprises the substeps of:

- 5 (i) generating a cube wall about each nodule candidate;
- (ii) determining an intersection volume, V_{ni} , corresponding to portions of the nodule region associated with the nodule candidate that intersect the cube wall;
- 10 (ii) removing the nodule candidate from the list when the fraction of the intersection volume, V_{ni} , over the volume of the nodule candidate, V_n , exceeds T_{vv} .

9. A method for analyzing a whole lung computed tomography scan as defined in Claim 7, wherein step (e) comprises the substeps of:

- (i) generating a cube wall about each nodule candidate;
- (ii) determining an intersection volume, V_{ni} , corresponding to portions of the nodule region associated with the nodule candidate that intersect the cube wall;
- 20 (ii) removing the nodule candidate from the list when the fraction of the intersection volume, V_{ni} , over the volume of the nodule candidate, V_n , exceeds T_{vv} .

25 10. A lung nodule detecting apparatus for analyzing a computed tomography scan of a whole lung for lung nodules, the lung nodule detecting apparatus comprising:

a detecting unit configured to:

- 30 (a) segment a first lung region and a second lung region from the computed tomography scan, the first lung region corresponding to lung parenchyma

of the lung and the second lung region corresponding to at least one of a pleural surface of the lung and a surface defined by vessels within the lung;

(b) generate an initial list of nodule candidates from the computed tomography scan within the first lung region, the list including at least a center location and an estimated size associated with each nodule candidate;

(c) generate a subimage for each nodule candidate in the initial list;

(d) selectively remove streaking artifacts from the subimage; and

(e) filter the nodule candidate identified on the initial list to eliminate false positives from the list.

11. A lung nodule detecting apparatus as defined by Claim 10, wherein for step (b) said detecting unit is configured to:

(i) threshold the first lung region;

(ii) label high density voxels foreground voxels to identify nodule candidate regions;

(iii) determine for each foreground voxel R_{MI} ;

(iv) select the local maximum \hat{R}_{MI} within a nodule candidate region;

(v) determine a limited extent criterion for each foreground voxel which corresponds to a \hat{R}_{MI} ;

(vi) generate the initial list of nodule candidates which satisfy the limited extent criterion, the list including at least N_c and \hat{R}_{MI} associated with the corresponding foreground voxel.

12. A lung nodule detecting apparatus as defined by Claim 10, wherein step (d) comprises the substeps of:

- (i) determine an amount of streaking artifact present in the sub-image; and
- (ii) filter the streaking artifact out from the subimage when the amount of the streaking artifact present in the sub-image exceeds T_{sar} .

- 5 13. A lung nodule detecting apparatus as defined by Claim 12, wherein the amount of streaking artifact present in the sub-image is calculated by a metric

$$S_m = \frac{1}{nmp} \sum_i^n \sum_j^m \sum_k^p (I(i,j,k) - I(i,j+1,k))^2$$

- 10 14. A lung nodule detecting apparatus as defined by Claim 12, further comprising a vertical median filter of size 1x3 to filter the streaking artifact.

- 15 15. A lung nodule detecting apparatus as defined by Claim 12, wherein T_{sar} is from about 20000 to about 80000.

16. A lung nodule detecting apparatus as defined by Claim 10, wherein step (e) comprises the substeps of:

- (i) determining for each nodule candidate a fraction, F_a , a surface of the
- 20 nodule candidate that is attached to other solid structures; and
- (ii) removing the nodule candidate from the list when the fraction exceeds T_a .

- 25 17. A lung nodule detecting apparatus as defined by Claim 10, wherein step (e) comprises the substeps of:

- (i) generating a cube wall about each nodule candidate;
- (ii) determining an intersection volume, V_{ni} , corresponding to portions of
- 30 the nodule region associated with the nodule candidate that intersect the cube wall;

(ii) removing the nodule candidate from the list when the fraction of the intersection volume, V_{ni} , over the volume of the nodule candidate, V_n , exceeds T_{vv} .

5 18. A lung nodule detecting apparatus as defined by Claim 16, wherein step (e) comprises the substeps of:

(i) generating a cube wall about each nodule candidate;

10 (ii) determining an intersection volume, V_{ni} , corresponding to portions of the nodule region associated with the nodule candidate that intersect the cube wall;

(ii) removing the nodule candidate from the list when the fraction of the
15 intersection volume, V_{ni} , over the volume of the nodule candidate, V_n , exceeds T_{vv} .

19. An article of manufacture for detecting lung nodules in a computed tomography scan of a whole lung, the article comprising:

20 a machine readable medium containing one or more programs which when executed implement the steps of:

(a) segmenting a first lung region and a second lung region from the computed tomography scan, the first lung region corresponding to lung parenchyma of the lung and the second lung region corresponding to at least one of a pleural
25 surface of the lung and a surface defined by vessels within the lung;

(b) generating an initial list of nodule candidates from the computed tomography scan within the first lung region, the list including at least a center location and an estimated size associated with each nodule candidate;

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(c) generating a subimage for each nodule candidate in the initial list;

(d) selectively removing streaking artifacts from the subimage; and

(e) filtering the nodule candidate identified on the initial list to eliminate false positives from the list.

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20. An article of manufacture for detecting lung nodules as defined by Claim 19, wherein step (b) comprises the substeps of:

(i) thresholding the first lung region;

10 (ii) labeling high density voxels foreground voxels to identify nodule candidate regions;

(iii) determining for each foreground voxel RMI;

(iv) selecting the local maximum \hat{R}_{MI} within a nodule candidate region;

(v) determining a limited extent criterion for each foreground voxel which

15 corresponds to a \hat{R}_{MI} ;

(vi) generating the initial list of nodule candidates which satisfy the limited extent criterion, the list including at least N_c and \hat{R}_{MI} associated with the corresponding foreground voxel.

20 21. An article of manufacture for detecting lung nodules as defined by Claim 19, wherein step (d) comprises the substeps of:

(i) determining an amount of streaking artifact present in the sub-image;

and

25 (ii) filtering the streaking artifact out from the subimage when the amount of the streaking artifact present in the sub-image exceeds T_{sar} .

22. An article of manufacture for detecting lung nodules as defined by Claim 21, wherein the amount of streaking artifact present in the sub-image is calculated by a
30 metric

$$S_m = \frac{1}{nmp} \sum_i^n \sum_j^m \sum_k^p (I(i,j,k) - I(i,j+1,k))^2$$

23. An article of manufacture for detecting lung nodules as defined by Claim 21,
wherein the filtering is performed by a vertical median filter of size 1x3.
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24. An article of manufacture for detecting lung nodules as defined by Claim 21,
wherein T_{sar} is from about 20000 to about 80000.
25. An article of manufacture for detecting lung nodules as defined by Claim 19,
10 wherein step (e) comprises the substeps of:
- (i) determining for each nodule candidate a fraction, F_a , a surface of the
nodule candidate that is attached to other solid structures; and
 - (ii) removing the nodule candidate from the list when the fraction exceeds
15 T_a .
26. An article of manufacture for detecting lung nodules as defined by Claim 19,
wherein step (e) comprises the substeps of:
- 20 (i) generating a cube wall about each nodule candidate;
 - (ii) determining an intersection volume, V_{ni} , corresponding to portions of
the nodule region associated with the nodule candidate that intersect the cube
wall;
 - 25 (ii) removing the nodule candidate from the list when the fraction of the
intersection volume, V_{ni} , over the volume of the nodule candidate, V_n , exceeds
 T_{vv} .
- 30 27. An article of manufacture for detecting lung nodules as defined by Claim 25,
wherein step (e) comprises the substeps of:

(i) generating a cube wall about each nodule candidate;

(ii) determining an intersection volume, V_{ni} , corresponding to portions of the nodule region associated with the nodule candidate that intersect the cube wall;

(ii) removing the nodule candidate from the list when the fraction of the intersection volume, V_{ni} , over the volume of the nodule candidate, V_n , exceeds T_{vv} .

28. A method for correlating a segmentation of 3-d images of a pulmonary nodule from a high-resolution computed tomography (CT) scans, the images being in a floating point pixel-format associated with a 6-dimensional parameter space and including a first image (im_1) obtained at time-1 and a second image (im_2) obtained at time-2, the method comprising the steps of:

- (a) selecting a first region-of-interest (ROI_1) for the nodule in the first image (im_1);
- (b) selecting a second region-of-interest (ROI_2) for the nodule in the second image (im_2);
- (c) registering the second region-of-interest (ROI_2) to the first region-of-interest (ROI_1) to obtain a transformed second region-of-interest (ROI_{2t});
- (d) separately segmenting both the nodule in the first region-of-interest (ROI_1) and the transformed second region-of-interest (ROI_{2t}); and
- (e) adjusting the first segmented nodule (S_1) and the second segmented nodule (S_2).

29. A method for correlating a segmentation of 3-d images as defined in Claim 28, wherein the first region-of-interest (ROI_1) is cubic and is selected to be about three times the size of the diameter of the nodule.

30. A method for correlating a segmentation of 3-d images as defined in Claim 28, wherein the second region-of-interest (ROI₂) is cubic and is selected to be about three times the size of the diameter of the nodule.

5 31. A method for correlating a segmentation of 3-d images as defined in Claim 28, wherein step (d) includes at least one of the following substeps of:

- (i) gray-level thresholding;
- (ii) morphological filtering for vessel removal; and
- (iii) plane clipping for separating a pleural wall.

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32. A method for correlating a segmentation of 3-d images as defined in Claim 31, wherein the gray-level thresholding is performed at an adaptive threshold level.

15 33. A method for correlating a segmentation of 3-d images as defined in Claim 32, wherein the adaptive threshold level is selected for each region-of-interest (ROI₁ and ROI₂) by:

determining a peak parenchyma value, v_p ;

determining a peak nodule value, v_n ;

20 calculating the adaptive threshold level as a midpoint between the peak parenchyma value, v_p , and the peak nodule value, v_n .

34. A method for correlating a segmentation of 3-d images as defined in Claim 33, further comprising the step of calculating an intensity histogram, $H(x)$ for determining the peak parenchyma value, v_p , and the peak nodule value, v_n .

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35. A method for correlating a segmentation of 3-d images as defined in Claim 34, wherein the intensity histogram, $H(x)$, is calculated between about -1024 HU and about 476 HU with a bin size of about 1.

36. A method for correlating a segmentation of 3-d images as defined in Claim 34, further comprising the substep of:
- 5 filtering the intensity histogram, $H(x)$, with a gaussian with standard deviation of about 25 HU prior to determining the peak parenchyma value, v_p , and the peak nodule value, v_n .
37. A method for correlating a segmentation of 3-d images as defined in Claim 34, wherein the intensity histogram, $H(x)$, is searched between about -1024 HU and
- 10 about -680 for the peak parenchyma value, v_p .
38. A method for correlating a segmentation of 3-d images as defined in Claim 34, wherein the intensity histogram, $H(x)$, is searched between about -227 HU and about -173 for the peak nodule value, v_n .
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39. A method for correlating a segmentation of 3-d images as defined in Claim 28, wherein registering the second region-of-interest (ROI_2) to the first region-of-interest (ROI_1) to obtain a transformed second region-of-interest (ROI_{2t}) comprises the substeps of:
- 20 (a) calculating initial rigid-body transformation parameters for a rigid-body transformation on the second region-of-interest (ROI_2);
- (b) determining the optimum rigid-body transformation parameters by calculating a registration metric between the first region-of-interest (ROI_1) and the rigid-body transformation on the second region-of-interest (ROI_2); and
- 25 (c) generating a registered image from the optimum rigid-body transformation parameters.

40. A method for correlating a segmentation of 3-d images as defined in Claim 39, wherein the registration metric is calculated by

transforming the second region-of-interest (ROI₂) with the initial rigid-body transformation parameters to obtain a transformed second region-of-interest

5 (ROI_{2t});

calculating the registration metric as a mean-squared-difference (MSD) between the transformed second region-of-interest (ROI_{2t}) and the first region-of-interest (ROI₁); and

10 searching for the minimum mean-squared-difference (MSD) in the 6-dimensional parameter space.

41. A method for correlating a segmentation of 3-d images as defined in Claim 40, wherein the transforming of the second region-of-interest (ROI₂) to obtain the transformed second region-of-interest (ROI_{2t}) is a mapping of a point v in 3-d space

15 to a point v' in transformed space defined by :

$$v' = R_x R_y R_z v + \begin{bmatrix} t_x \\ t_y \\ t_z \end{bmatrix}$$

wherein R_x , R_y , and R_z are rotation matrices defined as:

$$R_x = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos(r_x) & -\sin(r_x) \\ 0 & \sin(r_x) & \cos(r_x) \end{bmatrix}$$

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$$R_y = \begin{bmatrix} \cos(r_y) & 0 & \sin(r_y) \\ 0 & 1 & 0 \\ -\sin(r_y) & 0 & \cos(r_y) \end{bmatrix}$$

$$R_z = \begin{bmatrix} \cos(r_z) & -\sin(r_z) & 0 \\ \sin(r_z) & \cos(r_z) & 0 \\ 0 & 0 & 1 \end{bmatrix}.$$

42. A method for correlating a segmentation of 3-d images as defined in Claim 39,
 wherein said initial rigid-body transformation parameters include six parameters
 5 (tx,ty,tz,rx,ry,rz) respectively defined as translation in x, translation in y, translation in
 z, rotation about the x-axis, rotation about the y-axis, and rotation about the z-axis;
 wherein the initial rotation parameters (rx,ry,rz) are all set to zero; and the
 initial translation parameters (tx,ty,tz,) are set so that the nodule in the first region-of-
 interest (ROI₁) overlaps the nodule in the second region-of-interest (ROI₂)) during the
 10 initial calculation of the registration metric.

43. A method for correlating a segmentation of 3-d images as defined in Claim 40,
 wherein the mean-squared-difference (MSD) is gaussian weighted.

15 44. A method for correlating a segmentation of 3-d images as defined in Claim 31,
 wherein:

a first thresholded image (T₁) and a second thresholded image (T₂) are defined
 by gray-level thresholding prior to vessel removal and separating the pleural wall;
 and

20 step (e) is performed by comparing the segmented nodules and the thresholded
 images.

45. A method for correlating a segmentation of 3-d images as defined in Claim 44,
 wherein an active pixel is marked as one of:

- 25 a repeat nodule pixel;
- a nodule growth pixel;

a nodule atrophy pixel; and
a nodule missegmentation pixel.

46. A method for correlating a segmentation of 3-d images as defined in Claim 44,
5 wherein a foreground pixel in the first segmented nodule (S_1) is marked as a repeated
nodule pixel from the first region-of-interest (ROI_1) to the transformed second region-
of-interest (ROI_{2t}) when the corresponding pixel in second segmented nodule (S_2) and
the corresponding pixel in second thresholded image (T_2) are both foreground

10 47. A method for correlating a segmentation of 3-d images as defined in Claim 45,
wherein a foreground pixel in the first segmented nodule (S_1) is marked as a nodule
atrophy pixel when the corresponding pixel in second segmented nodule (S_2) is
background and the corresponding pixel in second thresholded image (T_2) is
background.

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48. A method for correlating a segmentation of 3-d images as defined in Claim 45,
wherein a foreground pixel in the first segmented nodule (S_1) is marked as a
missegmented pixel in the first region-of-interest (ROI_1) when the corresponding
pixel in second segmented nodule (S_2) is background and the corresponding pixel in
20 second thresholded image (T_2) is foreground.

49. A method for correlating a segmentation of 3-d images as defined in Claim 45,
wherein a foreground pixel in the second segmented nodule (S_2) is marked as a
repeated nodule pixel from the first region-of-interest (ROI_1) to the transformed
25 second region-of-interest (ROI_{2t}) when the corresponding pixel in first segmented
nodule (S_1) and the corresponding pixel in first thresholded image (T_1) are both
foreground.

50. A method for correlating a segmentation of 3-d images as defined in Claim 45, wherein a foreground pixel in the second segmented nodule (S_2) is marked as a nodule growth pixel when the corresponding pixel in first segmented nodule (S_1) is background and the corresponding pixel in first thresholded image (T_1) is background.

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51. A method for correlating a segmentation of 3-d images as defined in Claim 45, wherein a foreground pixel in the second segmented nodule (S_2) is marked as a missegmented pixel in the transformed second region-of-interest (ROI_{2t}) when the corresponding pixel in first segmented nodule (S_1) is background and the corresponding pixel in first thresholded image (T_1) is foreground.

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52. A registration apparatus for correlating a segmentation of 3-d images of a pulmonary nodule from a high-resolution computed tomography (CT) scans, the images being in a floating point pixel-format associated with a 6-dimensional parameter space and including a first image (im_1) obtained at time-1 and a second image (im_2) obtained at time-2, the registration apparatus comprising:

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a registration unit configured to:

(a) select a first region-of-interest (ROI_1) for the nodule in the first image (im_1);

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(b) select a second region-of-interest (ROI_2) for the nodule in the second image (im_2);

(c) register the second region-of-interest (ROI_2) to the first region-of-interest (ROI_1) to obtain a transformed second region-of-interest (ROI_{2t});

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(d) separately segment both the nodule in the first region-of-interest (ROI_1) and the transformed second region-of-interest (ROI_{2t}); and

(e) adjust the first segmented nodule (S_1) and the second segmented nodule (S_2).

53. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 52, wherein the first region-of-interest (ROI₁) is cubic and is selected to be about three times the size of the diameter of the nodule.
- 5 54. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 52, wherein the second region-of-interest (ROI₂) is cubic and is selected to be about three times the size of the diameter of the nodule.
55. A registration apparatus for correlating a segmentation of 3-d images as
10 defined in Claim 52, wherein for step (d) said registration unit is configured to:
- (i) gray-level threshold;
 - (ii) morphological filter to remove vessels; and
 - (iii) plane clip to separate a pleural wall.
- 15 56. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 55, wherein the gray-level threshold is performed at an adaptive threshold level.
57. A registration apparatus for correlating a segmentation of 3-d images as
20 defined in Claim 56, wherein the adaptive threshold level is selected for each region-of-interest (ROI₁ and ROI₂) by:
- determining a peak parenchyma value, v_p ;
 - determining a peak nodule value, v_n ;
 - calculating the adaptive threshold level as a midpoint between the peak
25 parenchyma value, v_p , and the peak nodule value, v_n .
58. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 57, wherein said registration unit is configured to calculate an

intensity histogram, $H(x)$ for determining the peak parenchyma value, v_p , and the peak nodule value, v_n .

59. A registration apparatus for correlating a segmentation of 3-d images as
5 defined in Claim 58, wherein the intensity histogram, $H(x)$, is calculated between
about -1024 HU and about 476 HU with a bin size of about 1.

60. A registration apparatus for correlating a segmentation of 3-d images as
defined in Claim 58, wherein said registration unit is configured to filter the intensity
10 histogram, $H(x)$, with a gaussian with standard deviation of about 25 HU prior to
determining the peak parenchyma value, v_p , and the peak nodule value, v_n .

61. A registration apparatus for correlating a segmentation of 3-d images as
defined in Claim 58, wherein the intensity histogram, $H(x)$, is searched between
15 about -1024 HU and about -680 for the peak parenchyma value, v_p .

62. A registration apparatus for correlating a segmentation of 3-d images as
defined in Claim 58, wherein the intensity histogram, $H(x)$, is searched between
about -227 HU and about -173 for the peak nodule value, v_n .

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63. A registration apparatus for correlating a segmentation of 3-d images as
defined in Claim 52, wherein said registration unit is configured to:

- (a) calculate initial rigid-body transformation parameters for a rigid-body
transformation on the second region-of-interest (ROI_2);
- 25 (b) determine the optimum rigid-body transformation parameters by
calculating a registration metric between the first region-of-interest (ROI_1) and the
rigid-body transformation on the second region-of-interest (ROI_2); and

(c) generate a registered image from the optimum rigid-body transformation parameters.

64. A registration apparatus for correlating a segmentation of 3-d images as
5 defined in Claim 63, wherein the registration metric is calculated by

transforming the second region-of-interest (ROI₂) with the initial rigid-body transformation parameters to obtain a transformed second region-of-interest (ROI_{2t});

calculating the registration metric as a mean-squared-difference (MSD)
10 between the transformed second region-of-interest (ROI_{2t}) and the first region-of-interest (ROI₁); and

searching for the minimum mean-squared-difference (MSD) in the 6-dimensional parameter space.

15 65. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 64, wherein the transforming of the second region-of-interest (ROI₂) to obtain the transformed second region-of-interest (ROI_{2t}) is a mapping of a point v in 3-d space to a point v' in transformed space defined by :

$$v' = R_x R_y R_z v + \begin{bmatrix} t_x \\ t_y \\ t_z \end{bmatrix}$$

20 wherein R_x , R_y , and R_z are rotation matrices defined as:

$$R_x = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos(r_x) & -\sin(r_x) \\ 0 & \sin(r_x) & \cos(r_x) \end{bmatrix}$$

$$R_y = \begin{bmatrix} \cos(r_y) & 0 & \sin(r_y) \\ 0 & 1 & 0 \\ -\sin(r_y) & 0 & \cos(r_y) \end{bmatrix}$$

$$R_z = \begin{bmatrix} \cos(r_z) & -\sin(r_z) & 0 \\ \sin(r_z) & \cos(r_z) & 0 \\ 0 & 0 & 1 \end{bmatrix}.$$

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66. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 63, wherein said initial rigid-body transformation parameters include six parameters (tx, ty, tz, rx, ry, rz) respectively defined as translation in x, translation in y, translation in z, rotation about the x-axis, rotation about the y-axis, and rotation
10 about the z-axis;

wherein the initial rotation parameters (rx, ry, rz) are all set to zero; and the initial translation parameters (tx, ty, tz) are set so that the nodule in the first region-of-interest (ROI_1) overlaps the nodule in the second region-of-interest (ROI_2) during the initial calculation of the registration metric.

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67. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 64, wherein the mean-squared-difference (MSD) is gaussian weighted.

20 68. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 55, wherein:

a first thresholded image (T_1) and a second thresholded image (T_2) are defined by gray-level thresholding prior to vessel removal and separating the pleural wall;
and

25 step (e) is performed by comparing the segmented nodules and the thresholded images.

69. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 68, wherein an active pixel is marked as one of:

- a repeat nodule pixel;
- 5 a nodule growth pixel;
- a nodule atrophy pixel; and
- a nodule missegmentation pixel.

70. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 69, wherein a foreground pixel in the first segmented nodule (S_1) is marked as a repeated nodule pixel from the first region-of-interest (ROI_1) to the transformed second region-of-interest (ROI_2) when the corresponding pixel in second segmented nodule (S_2) and the corresponding pixel in second thresholded image (T_2) are both foreground

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71. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 69, wherein a foreground pixel in the first segmented nodule (S_1) is marked as a nodule atrophy pixel when the corresponding pixel in second segmented nodule (S_2) is background and the corresponding pixel in second thresholded image (T_2) is background.

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72. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 69, wherein a foreground pixel in the first segmented nodule (S_1) is marked as a missegmented pixel in the first region-of-interest (ROI_1) when the corresponding pixel in second segmented nodule (S_2) is background and the corresponding pixel in second thresholded image (T_2) is foreground.

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73. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 69, wherein a foreground pixel in the second segmented nodule (S_2) is marked as a repeated nodule pixel from the first region-of-interest (ROI_1) to the transformed second region-of-interest (ROI_{2t}) when the corresponding pixel in first segmented nodule (S_1) and the corresponding pixel in first thresholded image (T_1) are both foreground.

74. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 69, wherein a foreground pixel in the second segmented nodule (S_2) is marked as a nodule growth pixel when the corresponding pixel in first segmented nodule (S_1) is background and the corresponding pixel in first thresholded image (T_1) is background.

75. A registration apparatus for correlating a segmentation of 3-d images as defined in Claim 69, wherein a foreground pixel in the second segmented nodule (S_2) is marked as a missegmented pixel in the transformed second region-of-interest (ROI_{2t}) when the corresponding pixel in first segmented nodule (S_1) is background and the corresponding pixel in first thresholded image (T_1) is foreground.

76. An article of manufacture for correlating a segmentation of 3-d images of a pulmonary nodule from a high-resolution computed tomography (CT) scans, the images being in a floating point pixel-format associated with a 6-dimensional parameter space and including a first image (im_1) obtained at time-1 and a second image (im_2) obtained at time-2, the article comprising:

a machine readable medium containing one or more programs which when executed implement the steps of:

- (a) selecting a first region-of-interest (ROI_1) for the nodule in the first image (im_1);
- (b) selecting a second region-of-interest (ROI_2) for the nodule in the second image (im_2);

(c) registering the second region-of-interest (ROI_2) to the first region-of-interest (ROI_1) to obtain a transformed second region-of-interest (ROI_{2t});

(d) separately segmenting both the nodule in the first region-of-interest (ROI_1) and the transformed second region-of-interest (ROI_{2t}); and

5 (e) adjusting the first segmented nodule (S_1) and the second segmented nodule (S_2).

77. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 76, wherein the first region-of-interest (ROI_1) is cubic and is
10 selected to be about three times the size of the diameter of the nodule.

78. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 76, wherein the second region-of-interest (ROI_2) is cubic and is selected to be about three times the size of the diameter of the nodule.

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79. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 76, wherein step (d) includes at least one of the following substeps of:

- (i) gray-level thresholding;
- 20 (ii) morphological filtering for vessel removal; and
- (iii) plane clipping for separating a pleural wall.

80. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 79, wherein the gray-level thresholding is performed at an adaptive threshold level.

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81. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 80, wherein the adaptive threshold level is selected for each region-of-interest (ROI_1 and ROI_2) by:

determining a peak parenchyma value, v_p ;

determining a peak nodule value, v_n ;

calculating the adaptive threshold level as a midpoint between the peak parenchyma value, v_p , and the peak nodule value, v_n .

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82. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 81, further comprising the step of calculating an intensity histogram, $H(x)$ for determining the peak parenchyma value, v_p , and the peak nodule value, v_n .

10 83. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 82, wherein the intensity histogram, $H(x)$, is calculated between about -1024 HU and about 476 HU with a bin size of about 1.

84. An article of manufacture for correlating a segmentation of 3-d images as
15 defined in Claim 82, further comprising the substep of:

filtering the intensity histogram, $H(x)$, with a gaussian with standard deviation of about 25 HU prior to determining the peak parenchyma value, v_p , and the peak nodule value, v_n .

20 85. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 82, wherein the intensity histogram, $H(x)$, is searched between about -1024 HU and about -680 for the peak parenchyma value, v_p .

86. An article of manufacture for correlating a segmentation of 3-d images as
25 defined in Claim 82, wherein the intensity histogram, $H(x)$, is searched between about -227 HU and about -173 for the peak nodule value, v_n .

87. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 76, wherein registering the second region-of-interest (ROI_2) to the first region-of-interest (ROI_1) to obtain a transformed second region-of-interest (ROI_{2t}) comprises the substeps of:

- 5 (a) calculating initial rigid-body transformation parameters for a rigid-body transformation on the second region-of-interest (ROI_2);
- (b) determining the optimum rigid-body transformation parameters by calculating a registration metric between the first region-of-interest (ROI_1) and the rigid-body transformation on the second region-of-interest (ROI_2); and
- 10 (c) generating a registered image from the optimum rigid-body transformation parameters.

88. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 87, wherein the registration metric is calculated by

- 15 transforming the second region-of-interest (ROI_2) with the initial rigid-body transformation parameters to obtain a transformed second region-of-interest (ROI_{2t});
- calculating the registration metric as a mean-squared-difference (MSD) between the transformed second region-of-interest (ROI_{2t}) and the first region-of-
- 20 interest (ROI_1); and
- searching for the minimum mean-squared-difference (MSD) in the 6-dimensional parameter space.

89. An article of manufacture for correlating a segmentation of 3-d images as
- 25 defined in Claim 88, wherein the transforming of the second region-of-interest (ROI_2) to obtain the transformed second region-of-interest (ROI_{2t}) is a mapping of a point v in 3-d space to a point v' in transformed space defined by :

$$v' = R_x R_y R_z v + \begin{bmatrix} t_x \\ t_y \\ t_z \end{bmatrix}$$

wherein R_x , R_y , and R_z are rotation matrices defined as:

$$R_x = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos(r_x) & -\sin(r_x) \\ 0 & \sin(r_x) & \cos(r_x) \end{bmatrix}$$

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$$R_y = \begin{bmatrix} \cos(r_y) & 0 & \sin(r_y) \\ 0 & 1 & 0 \\ -\sin(r_y) & 0 & \cos(r_y) \end{bmatrix}$$

$$R_z = \begin{bmatrix} \cos(r_z) & -\sin(r_z) & 0 \\ \sin(r_z) & \cos(r_z) & 0 \\ 0 & 0 & 1 \end{bmatrix}.$$

10 90. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 87, wherein said initial rigid-body transformation parameters include six parameters (tx, ty, tz, rx, ry, rz) respectively defined as translation in x, translation in y, translation in z, rotation about the x-axis, rotation about the y-axis, and rotation about the z-axis;

15 wherein the initial rotation parameters (rx, ry, rz) are all set to zero; and the initial translation parameters (tx, ty, tz) are set so that the nodule in the first region-of-interest (ROI₁) overlaps the nodule in the second region-of-interest (ROI₂)) during the initial calculation of the registration metric.

20 91. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 88, wherein the mean-squared-difference (MSD) is gaussian weighted.

92. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 79, wherein:

5 a first thresholded image (T_1) and a second thresholded image (T_2) are defined by gray-level thresholding prior to vessel removal and separating the pleural wall; and

step (e) is performed by comparing the segmented nodules and the thresholded images.

10 93. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 92, wherein an active pixel is marked as one of:

a repeat nodule pixel;

a nodule growth pixel;

a nodule atrophy pixel; and

15 a nodule missegmentation pixel.

94. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 93, wherein a foreground pixel in the first segmented nodule (S_1) is marked as a repeated nodule pixel from the first region-of-interest (ROI_1) to the
20 transformed second region-of-interest (ROI_2) when the corresponding pixel in second segmented nodule (S_2) and the corresponding pixel in second thresholded image (T_2) are both foreground

95. An article of manufacture for correlating a segmentation of 3-d images as
25 defined in Claim 93, wherein a foreground pixel in the first segmented nodule (S_1) is marked as a nodule atrophy pixel when the corresponding pixel in second segmented nodule (S_2) is background and the corresponding pixel in second thresholded image (T_2) is background.

96. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 93, wherein a foreground pixel in the first segmented nodule (S_1) is marked as a missegmented pixel in the first region-of-interest (ROI_1) when the
5 corresponding pixel in second segmented nodule (S_2) is background and the corresponding pixel in second thresholded image (T_2) is foreground.

97. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 93, wherein a foreground pixel in the second segmented nodule (S_2)
10 is marked as a repeated nodule pixel from the first region-of-interest (ROI_1) to the transformed second region-of-interest (ROI_{2t}) when the corresponding pixel in first segmented nodule (S_1) and the corresponding pixel in first thresholded image (T_1) are both foreground.

15 98. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 93, wherein a foreground pixel in the second segmented nodule (S_2) is marked as a nodule growth pixel when the corresponding pixel in first segmented nodule (S_1) is background and the corresponding pixel in first thresholded image (T_1) is background.

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99. An article of manufacture for correlating a segmentation of 3-d images as defined in Claim 93, wherein a foreground pixel in the second segmented nodule (S_2) is marked as a missegmented pixel in the transformed second region-of-interest (ROI_{2t}) when the corresponding pixel in first segmented nodule (S_1) is background
25 and the corresponding pixel in first thresholded image (T_1) is foreground.